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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/967,321	10/01/2001	Jonathon Michael Blackburn	0623.0860002/LBB/Y-W	4288

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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

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06/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/967,321	BLACKBURN ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 0407*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-14 and 16-27* is/are pending in the application.

4a) Of the above claim(s) *8-12,14 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,13,16-24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 8-12, 14 and 25 are withdrawn.

Claims 5-7 and 15 are cancelled.

Claims 1-4, 13, 16-24, 26 and 27 are examined below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-4, 13, 18-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al., 6,197,599.

Morin et al. discloses the invention substantially as claimed. As to claim 1, Morin discloses a method comprising

(a) inserting a marker DNA sequence in frame immediately preceding a stop codon of each of a plurality of target DNA sequences to form a plurality of modified DNA sequences which encode a plurality of modified amino acid sequence each comprising a marker moiety (col. 156, lines 20-25) (it is understood that a plurality of modified DNA

sequences are encoded, see for example col. 155, lines 29-30, disclosing producing of large quantities of hTRT using *Picha pastoris* expression vector pPICZ B, and col. 156, lines 16-18, disclosing a second *Picha pastoris* expression vector derived from pPICZ B);

(b) expressing the plurality of modified amino acid sequences from the plurality of modified DNA sequences (col. 156, lines 25-29);

(c) purifying and immobilizing each of the plurality of modified amino acid sequences into contact with a solid support wherein the marker moiety of the plurality of modified amino acid sequences is directly attached to the solid support (col. 43, lines 27-34), disclosing the isolation of the proteins by binding the $(HIS)_6$ to resins containing nickel ions, i.e., metal-chelate affinity chromatography, which is a direct attachment to the solid support, as is also disclosed by Applicants' specification) (the isolation step disclosed by Morin et al. is both the step of immobilizing and purifying in a single step, as is also disclosed by Applicants' specification), and

(d) washing said solid support to remove unbound proteins (col. 43, lines 30-34).

Moreover, while Morin et al. teaches use of the fusion protein system to isolate specific proteins and peptides (col. 43, lines 27-29), Morin et al. however does not teach that the bound proteins are in an array. This limitation is taught by Chin et al.

Chin et al. teaches that proteins immobilized on a solid support can be immobilized in an array, or specific position, so it can be identified by its position and further characterized thereby allowing for study of a wide variety of proteins in a single experiment by a large number of proteins on a support (col. 2, line 60 – col. 3, line 3.) It

would have been obvious to one of ordinary skill in the art at the time the invention was made to form the immobilized proteins in the Morin et al. invention in the form of an array as taught by Chin et al. for the advantage of identifying a protein based on its position and studying a wide variety of proteins in a single experiment for convenience.

As to the following claims, Morin et al. discloses the limitations as follows.

As to claim 2, the tag is a peptide sequence (col. 156, line 22).

As to claim 3, the tag allows for purification of the individual proteins in the array (col. 43, lines 27-29).

As to claim 4, the tag is inserted such that the start or stop codon for each of the proteins is replaced (column 156, lines 22-23).

As to claims 13 and 26, the array is used to immobilize specific antibodies (col. 43, lines 34-35).

As to claim 18, the protein array comprises kinases (col. 26, line 26.)

As to claim 19, the plurality of modified amino acid sequences are modified human amino acid sequences (see abstract, "human telomerase reverse transcriptase").

As to claim 20, Morin et al. teaches a FLAG marker moiety (col. 153, line 54.)

As to claims 21-23, the marker moiety is post-translationally modified (col. 49, line 44), such as addition of a lipid (col. 49, line 43), and the modified amino acid sequences are folded into the correct formation (col. 49, line 45.)

As to claim 27, Morin et al. teach using nickel ionon for metal-chelate affinity chromatography to bind polyhistidine tracts $(HIS)_6$.

2. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al, 6,197,599, and further in view of Ben-Bassat et al., 4,865,974.

Morin et al. in view of Chin et al. disclose the invention substantially as claimed (see above with respect to claim 1), except for the steps of digesting the target DNA sequence, annealing the marker DNA sequence and ligating the marker DNA sequence as claimed by Applicant. Although Morin et al. teaches that the hTRT stop codon is removed and replaced by vector sequences encoding for the Mye epitope and the His6 reporter tag (col. 156, lines 22-25), Morin et al. does not specifically disclose the steps for removing and replacing the DNA sequences. Ben-Bassat et al. teaches that the steps of digesting, annealing and ligating are well known in the art for removing and replacing DNA sequences.

Ben-Bassat et al. teaches that construction of suitable vectors containing the desired coding and control sequences employs standard ligation and restriction techniques which are well understood in the art (col 8, lines 3-6.) Bassat et al. teaches restriction enzymes for digestion of DNA sequences (col. 8, lines 9-10), annealing (col. 8, line 53) and ligation steps (col. 8, line 59.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the steps of digestions, annealing and ligation as taught by Ben-Bassat et al. for the steps of removing and

replacing DNA sequences in the Morin et al. method because Ben-Bassat et al. teaches that these steps are well known in the art for removing and replacing DNA sequences.

3. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al, 6,197,599, and further in view of Orr et al., 5,741,3645, and Nielsen et al., 6,350,853.

Morin et al. in view of Chin et al. disclose the invention substantially as claimed (see above), except for two markers, one immediately following a start codon and one immediately preceding a stop codon. Orr et al. discloses this limitation.

Orr et al. teaches the use of two flanking markers for the advantage of isolating region-specific DNA markers (col. 16, lines 40-44.) Moreover, Nielsen et al. teaches a marker sequence immediately following a start codon (col. 33, lines 23-26.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide two flanking markers as taught by Orr et al. in the Morin et al. method because Orr et al. teaches that it provides the advantage of isolating region-specific DNA markers, and it would have been obvious to one of ordinary skill in the art to provide the second marker immediately following a start codon as taught by Nielsen et al. as a known location for inserting a marker. Also, Applicant has not disclosed a use for inserting a marker immediate to the start codon that is a different use from that shown in the prior art.

Response to Arguments

Applicants' arguments filed April 4, 2007 has been considered but is not persuasive.

Applicants assert that Morin et al. on teaches insertion of a tag onto one particular DNA sequence, hTRT, as opposed to a plurality of target DNA sequences. However, it is understood that a plurality of modified DNA sequences are encoded because column 155, lines 29-30, discloses producing of large quantities of hTRT using *Picha pastoris* expression vector pPICZ B, and column 156, lines 16-18, then discloses a second *Picha pastoris* expression vector derived from pPICZ B.

Applicants also argue that Morin et al. do not teach purification and immobilization of the tagged sequence *in a single step*, wherein the proteins are directly attached to the solid support via the marker moiety. However, the Morin et al. disclosure of isolation of the tagged sequence by binding $(HIS)_6$ to resins containing nickel ions, i.e., metal-chelate affinity chromatograph, is a single step that is both an immobilization as well as purification (it is a purification because it removes other materials from the tagged sequence). This is the same as the disclosure of Applicants' invention. For the same reasons, Applicants' argument that Chin et al. and Orr et al. do not cure the deficiencies of Morin et al. is not persuasive because the Morin et al. disclosure is not deficient as argued by Applicants.

Applicants' argument regarding Orr et al. and the limitation of inserting a marker DNA sequence immediately following a start codon or immediately preceding a stop

codon as claimed is not persuasive because the Morin et al. reference, not the Orr et al. reference, is relied upon for these teachings.

Applicants also argue that the fluorescein moiety in the sequence taught by Nielsen et al. is not for the purpose of making tagged proteins on an array, but the marker sequence disclosed by Nielsen et al. is actually a short sequence containing a fluorescein moiety conjugated to a D-lysine residue on a short nucleobase sequence that binds to a region of the chloramphenical acetyltransferase gene for the purpose of inhibiting translation of CAT in vitro. This is not persuasive because the fluorescein moiety itself is not provided for the purpose of inhibiting translation of CAT in vitro, but rather is provided for the purpose of tagging the expressed protein for detection.

As to Applicants' argument regarding claim 27, Applicants' arguments are moot since the Little et al. and Stanley et al. references are not needed upon a review of the Morin et al. reference, which discloses the limitation recited in claim 27.

Conclusion

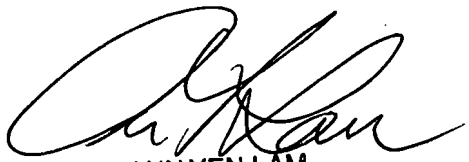
The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Riggs et al., 6,593,120, disclose a method inserting histidine tag immediately preceding a stop codon, or before a start codon and expressing the protein, and isolating the protein through immobilizing the histidine tag on a column with nickel

ions (col. 24, lines 23-24, col. 25, lines 13-19, col. 26, lines 37-47, col. 27, lines 33-36, and col. 5, lines 36-39).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



ANN YEN LAM
PATENT EXAMINER